Application No.: 09/846,727 Amendment dated April 26, 2005

Reply to Office Action dated January 26, 2005

Listing of Claims

This listing of claims will replace all prior versions, and listing, of claims in the Application.

1. (Previously Presented) A method for preparing a tracer composition comprising:

obtaining a ¹³C labeled Krebs cycle metabolite precursor that will produce an analyte; and

obtaining a deuterium source,

wherein gluconeogenensis is measured from a subject that was provided the precursor and the deuterium source, and produced the analyte, by comparison of the relative nuclear magnetic resonance profiles of the labeled components in the analyte.

- 2. (Original) The method of claim 1, wherein the analyte is ¹³C-glucose.
- 3. (Original) The method of claim 1, wherein the presursor is glucose, lactate or alanine.
- 4. (Original) The method of claim 1, wherein the deuterium source is deuterated water.
- 5. (Original) The method of claim 1, wherein the analyte is glucose deuterated in the 2, 5 and 6 positions, and any transformation that maintains the 2,5 and 6 positions in relation to one another.
- 6. (Original) The method of claim 1, wherein the analyte is $(1-6^{-13}C_2)$ -glucose.
 - 7. (Original) The method of claim 1, wherein the water is D_2O .
- 8. (Previously Presented) The method of claim 1, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.
- 9. (Original) The method of claim 1, wherein the analyte is ¹³C-labeled glucose with the label at the 2 or 5 positions, or at both positions.

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1. (Previously Presented) A method for preparing a tracer composition comprising:

obtaining a ¹³C labeled Krebs cycle metabolite precursor that will produce an analyte; and

obtaining a deuterium source,

wherein gluconeogenensis is measured from a subject that was provided the precursor and the deuterium source, and produced the analyte, by comparison of the relative nuclear magnetic resonance profiles of the labeled components in the analyte.

- 2. (Original) The method of claim 1, wherein the analyte is ¹³C-glucose.
- 3. (Original) The method of claim 1, wherein the presursor is glucose, lactose, lactate or alanine.
- 4. (Original) The method of claim 1, wherein the deuterium source is deuterated water.
- 5. (Original) The method of claim 1, wherein the analyte is glucose deuterated in the 2, 5 and 6 positions, and any transformation that maintains the 2,5 and 6 positions in relation to one another.
- 6. (Original) The method of claim 1, wherein the analyte is $(1-6^{-13}C_2)$ -glucose.
 - 7. (Original) The method of claim 1, wherein the water is D_2O .
- 8. (Previously Presented) The method of claim 1, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.
- 9. (Original) The method of claim 1, wherein the analyte is ¹³C-labeled glucose with the label at the 2 or 5 positions, or at both positions.

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17. (Currently Amended) A method for preparing a tracer composition comprising:

obtaining a deuterium source,

wherein gluconeogenensis is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance profiles of the deuterium components in the analyte The method of elaim 14, wherein the analyte is (1-6 ¹³C₂)-glucose.

- 18. (Previously Presented) The method of claim 16, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.
- 19. (Currently Amended) <u>A method for preparing a tracer composition</u> comprising:

obtaining a deuterium source;

wherein gluconeogenensis is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance profiles of the deuterium components in the analyte The method of elaim-14, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.

20. (Previously Presented) A method for preparing an isotopic metabolic flux tracer composition comprising:

providing a ¹³C labeled Krebs cycle metabolite precursor to a subject to produce an analyte;

obtaining a sample from the subject; and

measuring the nuclear magnetic resonance of the labeled tracers to determine the rate of gluconeogenesis.

- 21. (Original) The method of claim 20, wherein the analyte is ¹³C-glucose.
- 22. (Original) The method of claim 20, wherein the analyte is glucose labeled with ¹³C at positions 1 through 6, or combinations of two or more at any position.

- 23. (Original) The method of claim 20, wherein the analyte is $(1-6^{-13}C_2)$ -glucose.
- 24. (Original) The method of claim 20, wherein the sample is from blood, urine or tissue extracts.
- 25. (Original) The method of claim 20, further comprising the step of providing the subject with ¹³C₃-propionate.
- 26. (Original) The method of claim 20, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid, acetoacetic acid, beta-hydroxybutyric acid, a Krebs cycle pathway metabolite, and mixtures thereof.
- 27. (Original) The method of claim 20, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.
- 28. (Original) The method of claim 20, wherein the ¹³C Krebs cycle precursor is provided orally.
 - 29. 58. (Canceled).
- 59. (Previously Presented) A method for preparing a tracer composition comprising:

obtaining a deuterium source;

wherein gluconeogenensis is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance profiles of the deuterium components in the analyte, and

wherein the analyte is glucose deuterated in the 2, 5 and 6 positions, and any transformation that maintains the 2,5 and 6 positions in relation to one another, and

wherein the analyte is produced in the blood, urine or tissue.

60. (Previously Presented) The method of claim 1, wherein the analyte is produced in the blood, urine or tissue.

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61. (Previously Presented) A method for preparing an isotopic metabolic flux tracer composition comprising:

providing a ¹³C labeled Krebs cycle metabolite precursor to a subject to produce an analyte;

obtaining a sample from the subject; and

measuring the nuclear magnetic resonance of the labeled tracers to determine the rate of gluconeogenesis,

wherein the analyte is ¹³C-glucose.

- 62. (New) The method of claim 17, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.
- 63. (New) The method of claim 19, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.